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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,872	04/05/2001	Alan Solomon	044137-5029-US	3133

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,872	SOLOMON ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 32-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 32-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20050202*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Sworo

DETAILED ACTION

Status of the Claims

1. Claims 1-3 and 32-63 are pending.

Applicants' amendment filed February 22, 2005 is acknowledged. Applicants' response has been fully considered. Claims 3, 41-50 and 53-57 have been amended, and new claims 58-63 have been amended. Therefore, claims 1-3 and 32-63 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1, 2, 32-45, 50-52, 56 and 57 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicants' response at pages 7-17 of the amendment filed February 22, 2005.

3. The previous rejection of claims 37, 38 and 41-45 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at page 17 of the amendment filed February 22, 2005.

Infomalities

The disclosure is objected to because of the following informalities:

4. Fig. 3 contains an amino acid sequence of the first 58 residues of mouse AA amyloid, however, sequence listing containing this sequence is not provided. Applicants must comply with the requirements of the sequence rules (37 CFR 1.821-1.825) and submit a computer readable form (CRF) and a paper copy of sequence listing, and a statement that the content of the paper and CRF are the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3, 46-49, 53-55 and 62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising the synthetic fibrils, does not reasonably provide enablement for a vaccine composition comprising amyloid fibrils, an immunoglobulin light chain polypeptide, or a whole immunoglobulin light chain polypeptide. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 3, 46-49, 53-55 and 62 are directed to a vaccine composition comprising amyloid fibrils, an immunoglobulin light chain polypeptide, or a whole immunoglobulin light chain polypeptide. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention provides a method of removing amyloid deposits from a patient, comprising administering amyloid fibrils to generate an immune response that will promote the removal of in vivo amyloid fibrils; and also provides a vaccine or pharmaceutical composition comprising an amyloid fibril and a carrier (page 10, paragraph [0035]). There are no indicia that the present application enables the full scope of the claims in view of a vaccine composition comprising amyloid fibrils as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is

required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding various amyloid fibrils contained in a composition and used as a vaccine composition, which is not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification has demonstrated the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils (paragraphs [0128]-[0131]), it has not demonstrated the composition used as a vaccine to prevent the occurring of amyloid deposits, since vaccine is defined as a suspension of weakened, killed, or fragmented microorganisms or toxins or of antibodies or lymphocytes that is administered primarily to prevent disease (see Encyclopedia Britannica Online).

(3). The state of the prior art and relative skill of those in the art:

The prior art indicates the use of a pharmaceutical composition comprising amyloid fibril components (e.g., amyloid-β peptide or its variants) in the method of treating patients suffering from amyloidogenic disease to induce immune response against amyloid deposits in the patient (Schenk *et al.*, WO 99/27944), however, the prior art does not indicate the use of the composition as a vaccine. The general knowledge and level of the skill in the art do not

supplement the omitted description, the specification needs to provide specific guidance on the use of a composition comprising amyloid fibrils as a vaccine to prevent the occurring of amyloid deposits in a subject, and the protective effects of amyloid fibrils in the patient to be considered enabling.

(4). Predictability or unpredictability of the art:

The claims encompass a vaccine composition comprising amyloid fibrils, an immunoglobulin light chain polypeptide, or a whole immunoglobulin light chain polypeptide. While the specification indicates the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils (paragraphs [0128]-[0131]), it does not show the composition used as a vaccine to prevent the occurring of amyloid deposits. The specification has not demonstrated the protective effects of amyloid fibrils containing various proteins or the variants thereof in a subject. Therefore, the invention is highly unpredictable regarding the protective effects of the composition as a vaccine.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a vaccine composition comprising amyloid fibrils, an immunoglobulin light chain polypeptide, or a whole immunoglobulin light chain polypeptide. The specification indicates amyloid fibril encompasses fibrils of immunoglobulin light chain, amyloid A protein, beta 2-microglobulin, transthyretin, cystatin C variant, gelsolin, procalcitonin, PrP protein, amyloid beta-protein, ApoA, lysozyme, variants thereof or allelic variants thereof (paragraph 0078), and the use of a pharmaceutical composition containing immunoglobulin light chain variable region in the method of removing amyloid fibrils

(paragraphs [0128]-[0131]), it does not show the composition as a vaccine to prevent the occurring of amyloid deposits. Furthermore, there are no working examples demonstrating the protective effects of a composition containing amyloid fibrils. Since the specification fails to provide sufficient teaching on the use of a composition comprising amyloid fibrils as a vaccine, and the protective effect of the composition, it requires undue experimentation to assess the protective effect of the composition containing amyloid fibrils in a subject.

(6). Nature of the Invention

The scope of the claims encompasses a vaccine composition comprising amyloid fibrils, but the specification has not demonstrated the protective effects of a composition comprising various amyloid fibrils, an immunoglobulin light chain polypeptide, or a whole immunoglobulin light chain polypeptide in a subject. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the outcome is unpredictable regarding the protective effects of various amyloid fibrils, and the teachings in the specification are limited, therefore, it requires undue experimentation to assess the effects of a composition containing amyloid fibrils as a vaccine.

In response, applicants indicate the specification enables the vaccine compositions comprising mnyloid fibrils. Vaccine is generally defined as a preparation comprising an agent that is administered to a subject to stimulate an immune response that provide clinical benefit. A vaccine can be administered prior to the subject developing an illness, or, the vaccine can be administered after the subject has been in contact with the agent. An example of this is the rabies vaccine. The specification on pages 22-25 provides guidance for making and using vaccines

comprising amyloid fibrils, and Example D specifically teaches administering amyloid fibrils to a subject (page 14 of the response).

The response has been considered, however, the argument is not fully persuasive because the specification only indicates the use of a pharmaceutical composition containing amyloid fibrils (e.g., immunoglobulin light chain variable region) in the method of removing amyloid fibrils (paragraphs [0128]-[0131]), it does not show the composition used as a vaccine to prevent the occurring of amyloid deposits. Thus, it requires undue experimentation to assess the protective effect of the composition containing amyloid fibrils in a subject.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1, 2, 32-45, 50-52, 56-61 and 63 are rejected under 35 U.S.C. 102(e) as being anticipated by Schenk (U.S. Patent 6,875,434), which claims the benefits of provisional application 60/080,970, filed April 7, 1998.

Schenk teaches a pharmaceutical composition comprising an active agent (e.g., a fibril peptide, aggregate form of Aβ, Aβ42 and Aβ1-40; column 8, lines 30-33) that is effective to induce an immune response against amyloid component (claim 59); and a method for treating a disorder characterized by amyloid deposition in a mammalian subject by administering a pharmaceutical composition comprising an active agent (e.g., a fibril peptide, aggregate form of Aβ, Aβ42 and Aβ1-40) that is effective to induce an immune response against amyloid component (column 3. line 58-column 5, line 9; claims 1, 39, 40), where a fibril peptide or protein is derived from a fibril precursor protein which is known to be associated with certain forms of amyloid diseases and includes e.g., immunoglobulin light chain (AL), amyloid β protein precursor (Aβ) or fragments, mutants or proteolytic peptides thereof (column 18, lines 1-13; claims 2, 37, 50-52, 58, 60-61); and such fragments, or analogs can be synthesized by solid phase peptide synthesis or recombinant expression, or obtained from natural sources (column 20, lines 3-29; claims 32-36, 56, 57, 63). Example I indicates PDAPP transgenic mice, which exhibit Alzheimer's-like pathology and are considered to be an animal model for Alzheimer's disease, are treated with aggregated Aβ42 (AN1792), most of treated mice had no detectable amyloid in their brains at 13 months of age in contrast to control mice, all of which showed significant brain amyloid burden (Figs. 2 and 7; column 16, line 3-64; claims 41-45).

7. Claims 1, 32-45, 56, 57 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Schenk (WO 99/27944).

Schenk teaches a pharmaceutical composition comprising an active agent (e.g., aggregate form of Aβ, Aβ1–42 (AN1792) and Aβ1-40(AN1528)) that is effective to induce an immune response against amyloid component (pages 4 and 5; claim 59); and a method for treating patients suffering from amyloidogenic disease such as Alzheimer's disease by administering amyloid-beta peptide (Aβ) or variants thereof to induce immune response against amyloid deposit in the patient, where the amyloid-beta peptide can be administered in aggregated form, e.g., Aβ1-42 or Aβ1–40 (page 3, lines 1-29; page 8, lines 20-24; page 13, lines 28-33; page 43, line 24-page 45, line 20; page 50; Fig. 7; claims 1, 35-40, 56), and the PDAPP transgenic mice treated with one Aβ peptide (e.g., Aβ 1-42) has 81% less total Aβ level at 15 months than the PBS-immunized group (Tables 2-4, page 43, line 24-page 45, line 20; claims 41-45). The Aβ peptide and its fragments, or analogs can be synthesized by solid phase peptide synthesis or recombinant expression, or obtained from natural sources (page 15, lines 24-27; claims 32-34, 57).

In response to the Office Action dated January 14, 2003 (paper No. 11), applicants indicate Schenk teaches a method for treating patients suffering from amyloidogenic disease, comprising administering amyloid-beta peptide or variants thereof to induce an immune response against the amyloid deposits in the patient, while the claims of the present application are directed to a method of removing amyloid deposits from a subject comprising administering amyloid fibrils to the subject. The amyloid fibrils and the amyloid-beta peptide or variants thereof are structurally and functionally distinct products. Thus, the claims are not anticipated by Schenk (page 6 of the response filed July 14, 2003).

Applicants' response has been considered, however, the argument is not found persuasive because Schenk teaches the preparation and the use of aggregate form of Aβ, Aβ1–42 (AN1792) and Aβ1-40(AN1528) in the treatment of patients to induce immune response against amyloid deposit (page 50), where the aggregate form of Aβ, Aβ1–42 (AN1792) and Aβ1-40(AN1528) is amyloid fibrils, which is encompassed by the claimed invention. Thus, Schenk's reference anticipates the claimed invention.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
June 17, 2005

CHIH-MIN KAM
PATENT EXAMINER